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PEYRONIE'S DISEASE

Prevalence of Peyronie's Disease-Like Symptoms in Men Presenting With Dupuytren Contractures

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ABSTRACT

Introduction: Peyronie's disease (PD) and Dupuytren contractures (DC) are often comorbid and are believed to have a similar underlying pathophysiologic mechanism.

Aim: To investigate the prevalence of PD-like symptoms (PDLS) in men with DC.

Methods: From October 2013 to December 2016, men who were seen and evaluated for DC were offered the opportunity to participate in an anonymous survey. The survey assessed several basic demographic and sexual health factors and included items from the International Index of Erectile Function and the Erection Hardness Scale. Men who reported PDLS were asked a series of questions derived from the Peyronie's Disease Questionnaire and for their opinions on theoretical treatment modalities for sexual problems and penile deformity.

Main Outcome Measure: Prevalence of PDLS in men with DC.

Results: One hundred forty men with DC were invited to participate; 85 surveys were returned (response rate = 61%). Twenty-two respondents (26%, 95% confidence interval = 17−35) reported PDLS. Approximately one fourth of all respondents had an Erection Hardness Scale score lower than 3. The most common specific PDLS concerns were penile curvature (91%), length loss (55%), narrowing (36%), and hinging (32%). In men with PDLS, 73% felt at least a little bothered by the symptoms when attempting sexual activity and 40% reported having sex less frequently because of the symptoms. Just 27% of men with PDLS had ever used a treatment for a sexual concern. In terms of treatments for penile deformities, 64% of men with PDLS expressed an interest in treatment administered in the form of an in-office procedure; 41% were potentially amenable to a surgical procedure.

Conclusion: The prevalence of PDLS in men with DC is similar to the prevalence of DC in men diagnosed with PD. A substantial number of these men have distress and would consider standard-of-care treatments for PD. **Shindel AW, Sweet G, Thieu W, et al. Prevalence of Peyronie's Disease-Like Symptoms in Men Presenting With Dupuytren Contractures. Sex Med 2017;5:e135−e141.**

Key Words: Peyronie's Disease; Dupuytren Contractures; Screening; Treatment; Epidemiology; Survey Research

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INTRODUCTION

Peyronie's disease (PD; known historically as induratio penis plastica) is a potentially debilitating condition of penile deformity often accompanied by pain, curvature, loss of length, and erectile dysfunction (ED). The condition is believed to be related to abnormal collagen deposition within the penis.[1,2]

The prevalence of penile plaque in populations screened by trained examiners has been reported as high as 7% to 9%,[3,4] although the percentage of such patients who present for treatment is much smaller. PD is markedly more common in older men but has been reported in young men, including teenagers.[5,6] PD also is associated with other collagen deposition disorders such as tympanosclerosis, Lederhosen syndrome, and Dupuytren

contractures (DC) of the hands.[1,2] Gene expression analysis has suggested substantial overlap between DC and PD lesions,[7] indicating that a genetic predisposition to fibrotic conditions could contribute to the two conditions.

A clinical association between PD and DC was reported as long ago as 1828.[8] A 2011 study reported the prevalence of DC in men with PD at 22%.[9] Despite this established relation and emerging evidence on the prevalence of DC in PD, the prevalence of PD in men with DC has not, to our knowledge, been reported. In this pilot study we report on the prevalence of symptoms consistent with the diagnosis of PD in a population of men confirmed to have DC. We hypothesized that the prevalence of PD-like symptoms (PDLS) would be similar (eg, approximately 22%) to what has been reported for the prevalence of DC in PD. Exploratory end points included assessments of demographic and health factors and the relative bother and interest in therapies for men with PDLS.

METHODS

Study Population

Eligible men were identified from those presenting for evaluation at an orthopedic hand specialty clinic at a major academic medical center. An experienced orthopedic hand specialist evaluated all patients presenting with symptoms possibly consistent with DC. Those confirmed to have DC were offered the opportunity to participate in an anonymous survey. Interested men were provided a paper survey and given the option of completing and returning it immediately or mailing it to the research coordinator in a self-addressed stamped envelope. The study was open for enrollment from October 2013 to December 2016. To preserve anonymity, written informed consent was not obtained; informed consent was implied from completion and return of the survey. No inducement was provided. The institutional review board approved this study.

Survey

The survey instrument is presented in Appendix 1. We collected data on age, race, cigarette use, number of hands affected by DC, and comorbid conditions that have been associated with PD (ie, diabetes, hypertension, high cholesterol, gout, rheumatoid arthritis, nodules on the feet, or scarring of the inner ear). Men also were asked to complete the Erection Hardness Scale (EHS; four-point unipolar Likert scale)[10] and question 7 of the International Index of Erectile Function (IIEF) using a five-point unipolar Likert scale pertaining to the frequency of satisfactory sexual intercourse during the past 4 weeks with a sixth option for absence of sexual activity.[11]

Patients were asked if they had noted any changes in their penis after puberty; this time scale was selected to screen out congenital conditions such as chordee and normal changes in penile morphology that occur with puberty. Men who replied in the affirmative were considered at risk for PDLS and were asked another battery of questions regarding age of onset, specific type of changes noted, prior use of any sort of treatment to assist with sexual dysfunction, and willingness to consider treatment for penile morphologic changes. Men were asked to rate their willingness to use oral medications, office-based procedures, and surgical procedures to address the penile deformity; response options were based on a five-item bipolar Likert scale. Several items from the Peyronie's Disease Questionnaire (PDQ) also were included in this survey. Specifically, men were asked question 13 (pertaining to bother at last attempt to have sexual activity), question 14 (pertaining to having sex less often), and question 15 (pertaining to bother from having sex less often).[12] For sake of inclusion, all PDQ questions were modified from the original to be non-specific for vaginal intercourse.

Statistical Methods

Data analysis was conducted using R 3.3.1 (R Core Team, Vienna, Austria). Descriptive statistics (mean, SD, median, and range) were used for continuous variables, and categorical variables were summarized by number and percentage. Fisher exact test was used to test for the association between risk factors and PDLS. Given the sample size, multivariable analysis was not advisable. Any P values less than .05 were considered statistically significant and all statistical tests were two-sided. A 95% confidence interval for the prevalence of PDLS in this population was calculated using the normal approximation to the binomial distribution.

The primary outcome variable was prevalence of PDLS in men with confirmed DC. Secondary variables included specific manifestations of PDLS, degree of sexual bother (derived from elements of the EHS, IIEF, and PDQ), and interest in hypothetical therapies for PDLS.

RESULTS

Of men presenting for evaluation during the study enrollment period, 140 were confirmed to have DC and were invited to participate. Of these, 85 (61%) completed at least one question and returned the survey. Twenty-two men (26%) reported PDLS. The 95% confidence interval for estimation of PDLS in this population was 17% to 35%.

Demographic and comorbidity data are presented in Table 1. Men with and without PDLS were generally similar in their demographics and comorbidities. There were no statistically significant differences in these variables between men with and those without PDLS ($P > .05$).

Data on EHS scores and sexual satisfaction are presented in Table 2. The overall prevalence of an EHS score of 3 or 4 was similar between groups (75% and 77% for those without and with PDLS), although men in this group with PDLS tended to have an EHS score of 3 more frequently than those without PDLS. Sexual inactivity was slightly more common in men without PDLS (32% vs 18% for those without vs with PDLS,

Table 1. Demographic and comorbidity data

	No PD signs or symptoms (n = 63)	PD signs or symptoms (n = 22)	All patients (N = 85)	*P* value*
Demographics				
Current age (y)				.930
n	61	21	82	
Mean (SD)	65.1 (9.2)	65 (8.6)	65.1 (9)	
Median (range)	65 (44–84)	64 (46–76)	65 (44–84)	
Race, n (%)				
African-American or black	2 (3.2)	0	2 (2.4)	.706
American Indian, Native American, or Alaskan Native	1 (1.6)	1 (4.5)	2 (2.4)	
European-American or white	60 (95.2)	21 (95.5)	81 (95.3)	
Cigarette smoking, n (%)				>.999
No	61 (96.8)	22 (100)	83 (97.6)	
Yes	2 (3.2)	0	2 (2.4)	
Comorbidities, n (%)				
Hands with DC				.165
2 hands	18 (28.6)	3 (13.6)	21 (24.7)	
1 hand	27 (42.9)	15 (68.2)	42 (49.4)	
Not reported	18 (28.6)	4 (18.2)	22 (25.9)	
Diabetes				.274
No	52 (82.5)	21 (95.5)	73 (85.9)	
Yes	10 (15.9)	1 (4.5)	11 (12.9)	
Not reported	1 (1.6)	0	1 (1.2)	
High blood pressure				.806
No	36 (57.1)	12 (54.5)	48 (56.5)	
Yes	26 (41.3)	10 (45.5)	36 (42.4)	
Not reported	1 (1.6)	0	1 (1.2)	
High cholesterol				>.999
No	27 (42.9)	9 (40.9)	36 (42.4)	
Yes	36 (57.1)	13 (59.1)	49 (57.6)	
Inner ear scarring				.262
No	62 (98.4)	21 (95.5)	83 (97.6)	
Yes	0	1 (4.5)	1 (1.2)	
Not reported	1 (1.6)	0	1 (1.2)	
Nodules on feet				>.999
No	53 (84.1)	20 (90.9)	73 (85.9)	
Yes	7 (11.1)	2 (9.1)	9 (10.6)	
Not reported	3 (4.8)	0	3 (3.5)	
Gout				>.999
No	53 (84.1)	19 (86.4)	72 (84.7)	
Yes	8 (12.7)	3 (13.6)	11 (12.9)	
Not reported	2 (3.2)	0	2 (2.4)	
Rheumatoid arthritis				>.999
No	57 (90.5)	21 (95.5)	78 (91.8)	
Yes	3 (4.8)	1 (4.5)	4 (4.7)	
Not reported	3 (4.8)	0	3 (3.5)	

DC = Dupuytren contractures; PD = Peyronie's disease.
*P values are from a two-sample t-test for age and Fisher exact test for categorical variables.

respectively), although this difference did not achieve statistical significance ($P = .280$). The rate of satisfaction with sex "most" or "all" the time was similar between groups (64% for both groups).

Data on timing and nature of penile morphologic changes in men who reported PDLS are presented in Table 3. Curvature with erection was the most common complaint (n = 20, 91%), with loss of length (n = 12, 55%), shaft narrowing (n = 8,

Table 2. Data on EHS and sexual satisfaction

	No PD signs or symptoms (n = 63)	PD signs or symptoms (n = 22)	All patients (N = 85)	*P* value*
How hard does your penis get when you are sexually excited (turned on?)				.507
I have not had any sexual excitement	1 (1.6%)	0	1 (1.2%)	
My penis gets very hard and rigid (EHS score = 4)	30 (47.6%)	7 (31.8%)	37 (43.5%)	
My penis gets hard enough for sex but is not totally hard (EHS score = 3)	17 (27.0%)	10 (45.5%)	27 (31.8%)	
My penis gets larger and firm but not hard enough for sex (EHS score = 2)	9 (14.3%)	2 (9.1%)	11 (12.9%)	
My penis gets larger but not hard (EHS score = 1)	5 (7.9%)	3 (13.6%)	8 (9.4%)	
No erection at all	1 (1.6%)	0	1 (1.2%)	
When you had sex during the past month, how often was it satisfactory for you?				.187
Almost never or never	1 (1.6%)	0	1 (1.2%)	
A few times	1 (1.6%)	3 (13.6%)	4 (4.7%)	
Sometimes	1 (1.6%)	1 (4.5%)	2 (2.4%)	
Most time	11 (17.5%)	4 (18.2%)	15 (17.6%)	
Almost always or always	29 (46%)	10 (45.5%)	39 (45.9%)	
I have not had sex in the past month	20 (31.7%)	4 (18.2%)	24 (28.2%)	

EHS = Erection Hardness Scale; PD = Peyronie's disease.
*By Fisher exact test.

36%), hinging or weakness (n = 7, 32%), and pain with erection (n = 5, 23%) also common. At least some element of bother was reported by 17 (73%) of these men and 9 (41%) reported that they were having sex less often because of PDLS. Of these nine, five reported that they were "very" or "extremely" bothered.

Data on prior treatment for sexual concerns and theoretical interest in treatment in men who reported PDLS are presented in Table 4. Slightly more than one fourth of men reported having used a treatment for sexual concerns, with oral pharmacotherapy the most frequently used option. Patients reported being amenable (defined as "maybe," "probably yes," or "definitely yes") to considering therapy for PDLS in the form of an oral pill (19 patients, 86%), office procedure (14 patients, 64%), or surgical procedure (9 patients, 41%).

DISCUSSION

To our knowledge, these data represent the first analysis of the prevalence of bothersome, acquired changes in penile morphology in men with DC. Our response rate was 61%, which is high for an uncompensated survey. Consistent with our hypothesis, the rate of PDLS in this population was 26%. A substantial proportion of these men reported distress related to the condition and a willingness to consider treatment, including treatments that are currently available and supported by major guidelines (eg, intralesional collagenase and surgical correction of penile curvature).[13]

PD and DC are similar in that they are fibrotic disorders related to abnormal deposition of collagen in connective tissues.[1,2] Upregulation in genes related to collagen degradation, ossification, and myofibroblast differentiation has been reported in DC and PD tissues.[7] Given similarities in phenotype and genetic drivers of these two conditions, it is not surprising that these conditions often might be comorbid.

This cohort was predominantly Caucasian, which is consistent with the reported racial makeup of patients with PD and those with DC. The prevalence of various health conditions is within expected ranges for a cohort of men with mean age approximately 65 years; this also applies to the prevalence of ED in the study population[14] (estimated in this study by EHS score $\leq$ 2). PD has been historically associated with Caucasian race[15] and health factors including tobacco use.[3,16] PD also is often comorbid with risk factors for ED (eg, diabetes, hypertension, and hyperlipidemia).[16–18] Interestingly, one study suggested that hyperlipidemia and obesity (risk factors for ED) were inversely associated with PD.[15] We could not perform analysis on PDLS as a factor of ethnodemographic or health factors, but the existing literature implies that some of these conditions might have modulated the prevalence of PD in this cohort.

A substantial proportion of men from this cohort (with and without PDLS) had not been sexually active in the past month. The reason for absence of sexual activity was not elucidated in this study. Of those who were sexually active, most men in the two groups reported being usually or always satisfied with sexual encounters but a significant minority of men had less reliable satisfaction with sexual encounters. Although the reason for at least occasional lack of satisfaction with sex was not elucidated as

Table 3. Peyronie's symptoms in men reporting Peyronie's disease-like symptoms

How old (in years) were you when you first noticed the change in your erect penis? (n = 20)	
Mean (SD)	49.3 (16)
Median (range)	53.5 (11–72)
What changes have you noted in your penis when it is erect?	
Loss of length	
No	7 (31.8%)
Yes	12 (54.5%)
Not reported	3 (13.6%)
Lumps under the skin	
No	15 (68.2%)
Yes	4 (18.2%)
Not reported	3 (13.6%)
Curvature when erect	
No	1 (4.5%)
Yes	20 (90.9%)
Not reported	1 (4.5%)
Narrowing along the shaft	
No	12 (54.5%)
Yes	8 (36.4%)
Not reported	2 (9.1%)
Hinging or weakness of the shaft	
No	12 (54.5%)
Yes	7 (31.8%)
Not reported	3 (13.6%)
Pain with erection	
No	14 (63.6%)
Yes	5 (22.7%)
Not reported	3 (13.6%)
Pain with sex	
No	15 (68.2%)
Yes	4 (18.2%)
Not reported	3 (13.6%)
Something else	
Diminished intensity of orgasm	1 (4.5%)
Loss of girth or diameter. Used to bend left without lumps but was not evenly thick	1 (4.5%)
None reported	20 (90.9%)
Thinking about the last time you had or tried to have sex, how bothered were you by the change(s) in your penis?	
Not at all bothered	5 (22.7%)
A little bothered	8 (36.4%)
Moderately bothered	2 (9.1%)
Very bothered	5 (22.7%)
Extremely bothered	1 (4.5%)
Not reported	1 (4.5%)
Are you having sex less often because of the change in your penis?	
No	12 (54.5%)
Yes	9 (40.9%)
Not reported	1 (4.5%)
How bothered are you by having sex less often?	
Not at all bothered	0
A little bothered	1 (4.5%)
Moderately bothered	3 (13.6%)
Very bothered	4 (18.2%)
Extremely bothered	1 (4.5%)

a factor of the IIEF question, 40% of men with PDLS reported bother from less frequent sex specifically referable to the condition. Furthermore, 73% reported bother related to PDLS when engaging in sexual activity.

Relatively few patients had used any therapy for sexual concerns. More germane to the present analysis, many patients expressed interest in therapy for PDLS. Oral therapy for PDLS had the most interest; unfortunately, there is no oral PD therapy that has robust evidence of efficacy.[13] However, many patients reported that they would consider an in-office procedure (eg, intralesional injections) and/or surgical correction of deformity.[13]

Several important limitations must be discussed. Participation in this survey was voluntary; we have no reason to suspect that the population of men who did not complete it differed from the population that did but we cannot know this for certain. Patients who declined participation could have been satisfied with their sexual lives and disinterested in discussing it or they had no particular issues and did not see utility in participating. In either case, we acknowledge that this is a self-selected study but feel positively about the 61% response rate for an uncompensated survey. Given the small sample, there is a relatively wide confidence interval for our prevalence estimate. The 26% estimate of PDLS in men with DC should be viewed as preliminary. However, the data suggest that the prevalence of PDLS is consistent with our stated hypothesis. The relatively high event rate mitigates to some extent the limitations of the small sample; furthermore, the 95% confidence interval of PDLS with a lower bound of 17% indicates that even with conservative estimates a substantial proportion of men with DC are experiencing concerning symptoms relating to their penis. The sample size also limits the potential for analysis of demographics and comorbid conditions as modulators of the PD prevalence. Men who reported PDLS had neither a focused history nor physical examination to confirm the presence or absence of PD; we cannot estimate from these data the prevalence of actual PD. Regardless of how many of these men would have been confirmed to have PD, it is clear that a substantial number of men with DC have concerns about their penis and/or sexual health and are interested in available treatment options. In the population of men who did not have PDLS, approximately one third had not had sexual activity in the past month; whether these men had

Table 4. Treatment preferences in men with Peyronie's disease-like symptoms

Have you ever used a treatment to help you with problems having sex?	
No	15 (68.2%)
Yes	6 (27.3%)
Not reported	1 (4.5%)
What treatments have you used to help with problems having sex?	
Pills from a doctor (eg, Viagra, Levitra, Cialis)	
No	1 (4.5%)
Yes	5 (22.7%)
Not applicable or not reported	16 (72.7%)
Non-prescription pills (eg, herbals)	
No	4 (18.2%)
Yes	2 (9.1%)
Not applicable or not reported	16 (72.7%)
Penile injections (eg, Edex, Caverject, bi-mix)	
No	6 (27.3%)
Yes	0 (0%)
Not applicable or not reported	16 (72.7%)
Penis pump (vacuum erection device)	
No	6 (27.3%)
Yes	0 (0%)
Not applicable or not reported	16 (72.7%)
MUSE (pill that goes inside the penis)	
No	6 (27.3%)
Yes	0 (0%)
Not applicable or not reported	16 (72.7%)
Surgery	
No	5 (22.7%)
Yes	1 (4.5%)
Not applicable or not reported	16 (72.7%)
If there was a treatment for curvature, nodules, bends, or other deformities of the penis, would you use it if …	
Treatment was a pill to take by mouth?	
Definitely no	1 (4.5%)
Probably no	0
Maybe	8 (36.4%)
Probably yes	5 (22.7%)
Definitely yes	6 (27.3%)
Not reported	2 (9.1%)
Treatment required a procedure in a clinic office under local anesthetic?	
Definitely no	1 (4.5%)
Probably no	5 (22.7%)
Maybe	8 (36.4%)
Probably yes	2 (9.1%)
Definitely yes	4 (18.2%)
Not reported	2 (9.1%)
Treatment required a surgery in an operating room under general anesthesia?	
Definitely no	5 (22.7%)
Probably no	6 (27.3%)
Maybe	6 (27.3%)
Probably yes	1 (4.5%)
Definitely yes	2 (9.1%)
Not reported	2 (9.1%)

MUSE = medicated urethral suppository for erections.

experienced a prolonged period of abstinence that might have masked PDLS is unclear and cannot be gleaned from these data.

CONCLUSIONS

Many men with DC have bothersome symptoms consistent with PD. Hand specialists and primary care physicians should be aware of the relation between PD and DC and should inquire about sexual and penile health in men with DC. When appropriate, referral to a sexual medicine specialist should be initiated.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.esxm.2017.06.001.